Limits: **Entrez Date to 2002/8/30**

- Search History will be lost after eight hours of inactivity.
- Search numbers may not be continuous; all searches are represented.
- To save search indefinitely, click query # and select Save in My NCBI.
- To combine searches use #search, e.g., #2 AND #3 or click query # for more options.

Search	Most Recent Queries	Time	Result
#21	Search **aminopeptidase A binding peptide** Limits: **Entrez Date to 2002/8/30**	12:44:04	32
#20	Search **aminopeptidase A binding peptide**	12:40:23	43
#19	Search **aminopeptidase A-binding regulate endothelia**	12:40:06	0
#16	Search **Trepel M 2000**	12:38:44	2
#15	Search **marchion d 2000**	12:38:10	1
#14	Search **Marchio D 2000**	12:38:08	0
#11	Search **structure of a promoter and dna binding domain and activation domain** Limits: **Review**	09:58:15	31
#10	Search **strucutre of a promoter and DNA binding domain and activation domain** Limits: **Review**	09:57:44	0
#9	Search **promoter and DNA binding domain and activation domain** Limits: **Review**	09:57:15	96
#8	Search **promoter and DNA binding domain** Limits: **Review**	09:57:04	197
#5	Search **midkine promoter and transcriptional factor**	09:49:43	2
#2	Search **midkine promoter and transcriptional region**	09:48:28	8
#1	Search **midkin promter and transciprional region**	09:48:26	0

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NEWS 3 MAY 08 CA/CAplus Indian patent publication number format defined
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NEWS 5 MAY 21 BIOSIS reloaded and enhanced with archival data
NEWS 6 MAY 21 TOXCENTER enhanced with BIOSIS reload
NEWS 7 MAY 21 CA/CAplus enhanced with additional kind codes for German patents
NEWS 8 MAY 22 CA/CAplus enhanced with IPC reclassification in Japanese patents
NEWS 9 JUN 27 CA/CAplus enhanced with pre-1967 CAS Registry Numbers
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NEWS 11 JUN 29 STN Express, Version 8.2, now available
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NEWS 13 JUL 02 LMEDLINE coverage updated
NEWS 14 JUL 02 SCISEARCH enhanced with complete author names
NEWS 15 JUL 02 CHEMCATS accession numbers revised
NEWS 16 JUL 02 CA/CAplus enhanced with utility model patents from China

NEWS 17 JUL 16 CAplus enhanced with French and German abstracts
NEWS 18 JUL 18 CA/CAplus patent coverage enhanced
NEWS 19 JUL 26 USPATFULL/USPAT2 enhanced with IPC reclassification
NEWS 20 JUL 30 USGENE now available on STN
NEWS 21 AUG 06 CAS REGISTRY enhanced with new experimental property tags
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NEWS 23 AUG 06 FSTA enhanced with new thesaurus edition
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NEWS 26 AUG 27 Full-text patent databases enhanced with predefined patent family display formats from INPADOCDB
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NEWS 28 AUG 28 CAS REGISTRY enhanced with additional experimental spectral property data

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FILE 'CAPLUS' ENTERED AT 06:43:55 ON 06 SEP 2007

FILE 'BIOSIS' ENTERED AT 06:43:55 ON 06 SEP 2007
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=> phage (l) display
L1 11223 PHAGE (L) DISPLAY

=> aminopeptidae (w) A
L2 0 AMINOPEPTIDAE (W) A

=> aminopeptidase
L3 27126 AMINOPEPTIDASE

=> L1 and L3
L4 23 L1 AND L3

=> duplicate Remove L4
DUPLICATE PREFERENCE IS 'CAPLUS, BIOSIS'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):y
ENTER FILE NAMES OF DUPLICATES TO KEEP:caplus
PROCESSING COMPLETED FOR L4
L5 17 DUPLICATE REMOVE L4 CAPLUS (6 DUPLICATES REMOVED)

=> D L5 IBIB ABS 1-17

L5 ANSWER 1 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1248277 CAPLUS
DOCUMENT NUMBER: 146:22551
TITLE: Random mutagenesis, screening and selection of protease variants with altered sensitivity to activity modulators
INVENTOR(S): Koltermann, Andre; Kettling, Ulrich; Haupts, Ulrich; Coco, Wayne; Tebbe, Jan; Votsmeier, Christian; Scheidig, Andreas
PATENT ASSIGNEE(S): Direvo Biotech AG, Germany
SOURCE: Eur. Pat. Appl., 93pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1726643	A1	20061129	EP 2005-104543	20050527

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,

IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU

US 2006269538 A1 20061130 US 2006-441635 20060526

WO 2006125827 A1 20061130 WO 2006-EP62644 20060526

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: EP 2005-104543 A 20050527

US 2005-685566P P 20050527

US 2005-686021P P 20050531

AB The present invention provides a method for the selection of proteases with altered sensitivity to one or more activity-modulating substances. The method combines the provision of a protease library (i.e., phage display library) encoding polynucleotide sequences generated by using PCR mutagenesis, expression of the enzymes, screening of the library in the presence of one or several activity-modulating substances, selection of variants with altered sensitivity to one or several activity-modulating substances and isolation of those polynucleotide sequences that encode for the selected variants. In particular, mutant variants of human trypsin are disclosed.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:99599 CAPLUS

DOCUMENT NUMBER: 142:196523

TITLE: Antibodies bind to sulfated epitopes involving cell rolling, metastasis, inflammation, viral entry and autoimmune disease for diagnosis, prognosis and therapy

INVENTOR(S): Plaksin, Daniel; Levanon, Avigdor; Szanton, Esther; Hagay, Yocheved; Ben-Levy, Rachel; Nisgav, Yael; Szrajber, Tali; Kanfi, Yariv

PATENT ASSIGNEE(S): Savient Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 134 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005010153	A2	20050203	WO 2004-US21002	20040630
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004259406	A1	20050203	AU 2004-259406	20040630
CA 2536644	A1	20050203	CA 2004-2536644	20040630
EP 1649001	A2	20060426	EP 2004-777308	20040630
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
BR 2004011945	A	20061024	BR 2004-11945	20040630
MX 2006PA00252	A	20061215	MX 2006-PA252	20060105
IN 2006DN00485	A	20070817	IN 2006-DN485	20060130

PRIORITY APPLN. INFO.: US 2003-611238 A 20030630
WO 2004-US21002 W 20040630

AB The present invention provides antibodies or fragments (e.g. scFv antibodies) thereof that bind to cancer cells and is important in physiol. phenomena, such as cell rolling and metastasis. The antibodies bind to sulfated epitope of PSGL-1; GPIb; .alpha.-2 antiplasmin; aminopeptidase B; CC chemokine receptor; seven-transmembrane segment receptor; coagulation factor V, VIII, and IX; fibrinogen .gamma. chain; heparin cofactor II; secretogranin I and II; vitronectin; amyloid precursor;, cholecystokinin;, .alpha.-choriogonadotropin; complement C4; dermatan sulfate proteoglycan; fibronectin and castrin. Therapeutic and diagnostic methods and compns. using such antibody fragments thereof are also provided. The methods and compns. according to the present invention can be used in targeting therapeutic agents and in diagnosis, prognosis, and staging of and therapy for such diseases as cancer, including tumor growth and metastasis, leukemia, auto-immune disease, and inflammatory disease. Also provided is a library of Ig binding domains having a diverse antigen-binding domain for complementary binding, wherein the library has diversity only in heavy chain CDR3.

L5 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:283178 CAPLUS
DOCUMENT NUMBER: 142:353888
TITLE: Antibodies and fragments specific to sulfated epitope of PSGL-1, GPIb and/or CCR5 for diagnosis and therapy of cancer, autoimmune disease and inflammation
INVENTOR(S): Plaksin, Daniel; Levanon, Avigdor; Szanton, Esther; Hagay, Yocheved; Ben-levy, Rachel; Nisgav, Yael; Kanfi, Yariv
PATENT ASSIGNEE(S): Israel
SOURCE: U.S. Pat. Appl. Publ., 74 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005069955	A1	20050331	US 2004-880922	20040630
US 2005266009	A1	20051201	US 2005-166740	20050627

PRIORITY APPLN. INFO.: US 2003-484061P P 20030630
US 2004-880922 A2 20040630

AB The present invention provides antibodies or fragments thereof that bind to cancer cells and is important in physiol. phenomena, such as cell rolling and metastasis. Therapeutic and diagnostic methods and compns. using such antibody fragments thereof are also provided. The methods and compns. according to the present invention can be used in targeting therapeutic agents and in diagnosis, prognosis, and staging of and therapy for such diseases as cancer, including tumor growth and metastasis, leukemia, autoimmune disease, and inflammatory disease. Also provided is a library of Ig binding domains having a diverse antigen-binding domain for complementary binding, wherein the library has diversity only in heavy chain CDR3.

L5 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1000913 CAPLUS
DOCUMENT NUMBER: 142:50746
TITLE: ~~Display of biologically~~ functional insecticidal toxin on the surface of .lambda. phage
AUTHOR(S): Vilchez, Susana; Jacoby, Juliette; Ellar, David J.
CORPORATE SOURCE: Department of Biochemistry, Cambridge University, Cambridge, UK
SOURCE: Applied and Environmental Microbiology (2004), 70(11),

6587-6594
CODEN: AEMIDF; ISSN: 0099-2240
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The successful use of Bacillus thuringiensis insecticidal toxins to control agricultural pests could be undermined by the evolution of insect resistance. Under selection pressure in the lab., a no. of insects have gained resistance to the toxins, and several cases of resistance in the diamondback moth have been reported from the field. The use of protein engineering to develop novel toxins active against resistant insects could offer a soln. to this problem. The display of proteins on the surface of phages has been shown to be a powerful technol. to search for proteins with new characteristics from combinatorial libraries. However, this potential of phage display to develop Cry toxins with new binding properties and new target specificities has hitherto not been realized because of the failure of displayed Cry toxins to bind their natural receptors. In this work we describe the construction of a display system in which the Cry1Ac toxin is fused to the amino terminus of the capsid protein D of bacteriophage lambda. The resultant phage was viable and infectious, and the displayed toxin interacted successfully with its natural receptor.
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 17 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:477650 BIOSIS
DOCUMENT NUMBER: PREV200510269554
TITLE: A Plasmodium falciparum aminopeptidase interacts with human erythrocyte spectrin.
AUTHOR(S): Coetzer, Theresa L. [Reprint Author]; Lauterbach, Sonja B.
CORPORATE SOURCE: Univ Witwatersrand, Johannesburg, Gauteng, South Africa
SOURCE: Blood, (NOV 16 2004) Vol. 104, No. 11, Part 1, pp. 441A.
Meeting Info.: 46th Annual Meeting of the American-Society-of-Hematology. San Diego, CA, USA. December 04 -07, 2004. Amer Soc Hematol.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 2005
Last Updated on STN: 16 Nov 2005
AB Malaria is one of the world's major health problems, causing millions of deaths every year, primarily in Africa. The disease is caused by

Plasmodium parasites, which invade and destroy human erythrocytes. Of the four species infectinghumans, Plasmodium falciparum is responsible for the greatest morbidity and mortality burden. The erythrocyte membrane plays a vital role in all aspects ofthe pathogenic phase of the parasite's life cycle and the protein-protein interactions between host and parasite are a key focus of research. Spectrin is the main structural protein in the erythrocyte membrane skeleton and phage-display technology was used to probe the interaction between P falciparum peptide fragments and human erythrocyte spectrin. A phage-display library was constructed by isolating mRNA from P falciparum strain FCR-3, which was reverse transcribed using two-base anchored oligodT primers. Linkers facilitating directional cloning were added to the cDNA, followed by insertion into a gene encoding the I OB capsid protein of the T7 bacteriophage vector. The vector was packagedinto viral particles and the library amplified using Escherichia coli as a host. The presence and size of inserts were determined by PCR amplification withT7 bacteriophage vector arm specific primers. Human erythrocyte membranes were prepared from whole blood by hypotonic lysis and spectrin was extracted witha low ionic strength buffer and purified by size exclusion chromatography. The protein was biotinylated, immobilized on streptavidin-coated magnetic beads and biopanned against the phage library. Bound phage were elated and amplifiedin E coli for three additional rounds of biopanning to eliminate non-specificprotein-protein interactions. The P falciparum cDNA inserts of interacting phage were sequenced and compared to the PlasmoDB database. One of the sequenceswas identified as a putative aminopeptidase (PFI1570c), which has a 30.7% homology to a human aspartyl aminopeptidase, an enzyme catalysing the release of N-terminal amino acids from a peptide. The parasite protein contains a putative transmembrane domain at the C terminal end and is larger than the human form, with an estimated molecular weight of 65 kD. Several features that are critical for enzyme activity are conserved in the P falciparum aminopeptidase. These include twelve amino acids (four histidine, three glutamic acid and five aspartic acid residues), which are involved in the binding of catalytic zinc ionsin the active site, as well as a putative N-myristoylation site and phosphorylation sites for casein kinase 11 and protein kinase C. Interestingly, the peptide fragment that bound to spectrin in the initial phage display screening, corresponds to a 33 amino acid fragment that is not found in the human aspartylaminopeptidase. This suggests an evolutionary development of the parasite that allows the protease to bind to human spectrin. Mass spectrometry and microarray data from the PlasmoDB database indicate that the protein is present at the erythrocyte membrane and is expressed in all the developmental stages of theparasite's erythrocytic life cycle. During the trophozoite stage the parasitemodifies the erythrocyte membrane to allow transport of nutrients and waste products, The

aminopeptidase could cleave spectrin and destabilise the membraneskeleton to facilitate the insertion of parasite protein channels during development. It may also play a role in proteolysis of the skeleton to enable the release of schizonts from infected erythrocytes.

L5 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:991150 CAPLUS
DOCUMENT NUMBER: 140:35913
TITLE: Breast homing peptides binding to aminopeptidase P in beast vasculature identified by phage display and use thereof as targeting drugs for breast cancer treatment
INVENTOR(S): Ruoslahti, Erkki; Essler, Markus
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 30 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003232762	A1	20031218	US 2002-158566	20020529
PRIORITY APPLN. INFO.:			US 2002-158566	20020529

AB The present invention provides a method of directing a moiety to breast vasculature in a subject by administering to the subject a conjugate which contains a moiety linked to a homing mol. that selectively homes to breast vasculature, whereby the moiety is directed to breast vasculature. In one embodiment, the homing mol. is a peptide contg. the amino acid sequence PGPEGAG, or a peptidomimetic thereof. The above peptide is derived from a cyclic nonapeptide, CPGPEGAGC, isolated from a T7 phage CX7C library, where C is cysteine and X is any amino acid. This cyclic peptide CPGPEGAGC homes to normal breast tissue with a 100-fold selectivity over nontargeted phage. Specifically, it binds to the vascular endothelium in the breast but not in other tissues, and binds to the vasculature of hyperplastic and malignant lesions in transgenic breast cancer mice. Furthermore, the aminopeptidase P is identified as the receptor for cyclic CPGPEGAGC breast homing and the binding of aminopeptidase P to insolubilized CPGPEGAGC can be blocked by its free cognate synthetic peptide, or apstatin (a synthetic inhibitor of aminopeptidase P), or an anti-aminopeptidase P antibody. In contrast, the anti-aminopeptidase P antibody does not block the breast homing of another peptide CRSS, which might bind distinct target receptors in breast tissue. This breast homing peptides may be

useful in designing drugs for the prevention and treatment of breast cancer.

L5 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:241889 CAPLUS
DOCUMENT NUMBER: 138:268070
TITLE: Engineered protein binding domains and methods and systems for their design and use
INVENTOR(S): Gonzalez, Cayetano; Lacroix, Emmanuel; Reina, Jose; Serrano, Luis
PATENT ASSIGNEE(S): Germany
SOURCE: U.S. Pat. Appl. Publ., 67 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003059827	A1	20030327	US 2001-805353	20010313

PRIORITY APPLN. INFO.: US 2001-805353 20010313

AB The present invention rapidly and efficiently provides proteins engineered to bind to arbitrary target proteins requiring only knowledge of the amino acid sequences of short portions of the target proteins (for example, either the amino or the carboxy termini). This invention provides such proteins as well as methods and systems for their design, synthesis and use, and esp. provides for use of a plurality of binding proteins in array format. The engineering methods of the present invention take a precursor protein known to already bind to a short peptide and engineer alterations in precursor proteins so that it binds to a new target peptide by using computer-assisted mol. design techniques and optional assay for actual binding. The invention also provides arrays and libraries of binding proteins and methods of using binding proteins. Redesign of the PDZ domain of PSD-95 is described.

L5 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:185320 CAPLUS
DOCUMENT NUMBER: 136:242932
TITLE: Identification of peptide ligands for specific cell types by phage display for use in drug targeting and control of biological processes
INVENTOR(S): Arap, Wadih; Pasqualini, Renata
PATENT ASSIGNEE(S): Board of Regents, the University of Texas System, USA
SOURCE: PCT Int. Appl., 311 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002020769	A1	20020314	WO 2001-US27692	20010907
WO 2002020769	A9	20030904		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
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CA 2421271	A1	20020314	CA 2001-2421271	20010907
AU 200188843	A	20020322	AU 2001-88843	20010907
EP 1322755	A1	20030702	EP 2001-968603	20010907
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004508045	T	20040318	JP 2002-525776	20010907
CA 2458047	A1	20030320	CA 2002-2458047	20020830
WO 2003022991	A2	20030320	WO 2002-US27836	20020830
WO 2003022991	A3	20041028		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
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AU 2002323543	A1	20030324	AU 2002-323543	20020830
EP 1497314	A2	20050119	EP 2002-757531	20020830
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CA 2496938	A1	20040311	CA 2002-2496938	20021030
WO 2004020999	A1	20040311	WO 2002-US34987	20021030
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AU 2002364501	A1	20040319	AU 2002-364501	20021030
EP 1546714	A1	20050629	EP 2002-799873	20021030
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US 2004170955	A1	20040902	US 2003-363204	20031006
US 2005003466	A1	20050106	US 2004-784537	20040223
US 2006094672	A1	20060504	US 2004-489071	20041013
US 2006239968	A1	20061026	US 2006-530168	20060223

PRIORITY APPLN. INFO.: US 2000-231266P P 20000908
US 2001-765101 A 20010117
WO 2001-US27692 W 20010907
WO 2002-US27836 W 20020830
WO 2002-US34987 W 20021030

AB The present invention concerns methods and compns. for in vivo and in vitro targeting. A large no. of targeting peptides directed towards human organs, tissues or cell types are disclosed. The peptides are of use for targeted delivery of therapeutic agents, including but not limited to gene therapy vectors. A novel class of gene therapy vectors is disclosed. Certain of the disclosed peptides have therapeutic use for inhibiting angiogenesis, inhibiting tumor growth, inducing apoptosis, inhibiting pregnancy or inducing wt. loss. Methods of identifying novel targeting peptides in humans, as well as identifying endogenous receptor-ligand pairs are disclosed. Methods of identifying novel infectious agents that are causal for human disease states are also disclosed. A novel mechanism for inducing apoptosis is further disclosed.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:185278 CAPLUS
DOCUMENT NUMBER: 136:241645
TITLE: Adenoviral targeting and manipulation of immune system response using targeting peptides
INVENTOR(S): Arap, Wadih; Pasqualini, Renata
PATENT ASSIGNEE(S): Board of Regents, the University of Texas System, USA
SOURCE: PCT Int. Appl., 86 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002020724	A2	20020314	WO 2001-US28045	20010907
WO 2002020724	A3	20020711		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2421200	A1	20020314	CA 2001-2421200	20010907
AU 200190663	A	20020322	AU 2001-90663	20010907
EP 1315512	A2	20030604	EP 2001-970682	20010907
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004536020	T	20041202	JP 2002-525731	20010907
CA 2496938	A1	20040311	CA 2002-2496938	20021030
WO 2004020999	A1	20040311	WO 2002-US34987	20021030
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002364501	A1	20040319	AU 2002-364501	20021030
EP 1546714	A1	20050629	EP 2002-799873	20021030
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
US 2006094672	A1	20060504	US 2004-489071	20041013
US 2006239968	A1	20061026	US 2006-530168	20060223
PRIORITY APPLN. INFO.:			US 2000-231266P	P 20000908
			US 2001-765101	A 20010117
			US 2001-97651	A 20010117
			WO 2001-US28045	W 20010907

WO 2002-US27836 A 20020830
WO 2002-US34987 W 20021030

AB The present invention concerns compns. and methods relating to the identification and use of targeting peptides. Such targeting peptides selectively home to specific organs or tissues in vivo. The novel targeting sequences disclosed herein are of use for the targeted delivery of various therapeutic agents to the targeted organ or tissue. In particular embodiments, the present invention concerns bispecific targeting reagents comprising an organ targeting peptide attached to a mol., such as a Fab fragment, that binds to a gene therapy vector or other therapeutic agent. In alternative embodiments, bispecific targeting peptides contg. an organ targeting moiety and a gene therapy or therapeutic agent targeting moiety may be obtained and used for targeted delivery. Other embodiments concern modulation of host immune system function through the targeted delivery of antigens or other mols. to lymph nodes. Numerous examples of targeting peptide sequences against adenovirus or lymph node tissue are disclosed herein.

L5 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2002:200870 CAPLUS
DOCUMENT NUMBER: 137:98834
TITLE: Molecular specialization of breast vasculature: a breast-homing phage-displayed peptide binds to aminopeptidase P in breast vasculature
AUTHOR(S): Essler, Markus; Ruoslahti, Erkki
CORPORATE SOURCE: Cancer Research Center, The Burnham Institute, La Jolla, CA, 92037, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2002), 99(4), 2252-2257
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In vivo phage display identifies peptides that selectively home to the vasculature of individual organs, tissues, and tumors. Here the authors report the identification of a cyclic nonapeptide, CPGPEGAGC, which homes to normal breast tissue with a 100-fold selectivity over nontargeted phage. The homing of the phage is inhibited by its cognate synthetic peptide. Phage localization in tissue sections showed that the breast-homing phage binds to the blood vessels in the breast, but not in other tissues. The phage also bound to the vasculature of hyperplastic and malignant lesions in transgenic breast cancer mice. Expression cloning with a phage-displayed cDNA library yielded a phage that specifically bound to the breast-homing peptide. The cDNA insert was homologous to a fragment of

aminopeptidase P. The homing peptide bound aminopeptidase P from malignant breast tissue in affinity chromatog. Antibodies against aminopeptidase P inhibited the in vitro binding of the phage-displayed cDNA to the peptide and the in vivo homing of phage carrying the peptide. These results indicate that aminopeptidase P is the receptor for the breast-homing peptide. This peptide may be useful in designing drugs for the prevention and treatment of breast cancer.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 2002:915593 CAPLUS

DOCUMENT NUMBER: 138:252269

TITLE: Probing the structural and molecular diversity of tumor vasculature

AUTHOR(S): Pasqualini, Renata; Arap, Wadih; McDonald, Donald M.

CORPORATE SOURCE: Dept of Genitourinary Medical Oncology, M.D. Anderson Cancer Center, The University of Texas, Houston, TX, 77030, USA

SOURCE: Trends in Molecular Medicine (2002), 8(12), 563-571 CODEN: TMMRCY; ISSN: 1471-4914

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. The mol. diversity of the vasculature provides a rational basis for developing targeted diagnostics and therapeutics for cancer. Targeted imaging agents would offer better localization of primary tumors and metastases, and targeted therapies would improve efficacy and reduce side effects. The development of targeted pharmaceuticals requires the identification of specific ligand-receptor pairs, and knowledge of their cellular distribution and accessibility. Using in vivo phage display, a technique by which we can identify organ-specific and disease-specific proteins expressed on the endothelial surface, it is now possible to decipher the mol. signature of blood vessels in normal and diseased tissues. These studies have already led to the identification of peptides that target the normal vasculature of the brain, kidney, pancreas, lung and skin, as well as the abnormal vasculature of tumors, arthritis and atherosclerosis. Membrane dipeptidase in the lungs, interleukin-11 receptor in the prostate, and aminopeptidase N in tumors are examples of mol. targets on blood vessels. Corresponding confocal-microscopic imaging and ultrastructural studies are providing a more complete understanding of the cellular abnormalities of tumor blood vessels, and the distribution and accessibility of potential targets. The combined approach offers a strategy for creating a ligand-receptor map of

the human vasculature, and forms a foundation for the development and application of targeted therapies in cancer and other diseases. In vivo phage display is being used to characterize the mol. heterogeneity of blood vessels and to develop targeted therapies and imaging agents for use in cancer and other diseases.

REFERENCE COUNT: 82 THERE ARE 82 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 3

ACCESSION NUMBER: 2001:590903 CAPLUS

DOCUMENT NUMBER: 136:212397

TITLE: Mapping the epitope in cadherin-like receptors involved in Bacillus thuringiensis Cry1A toxin interaction using phage display

AUTHOR(S): Gomez, Isabel; Oltean, Daniela I.; Gill, Sarjeet S.; Bravo, Alejandra; Soberon, Mario

CORPORATE SOURCE: Instituto de Biotecnologia, Departamento de Microbiologia Molecular, Universidad Nacional Autonoma de Mexico, Mexico, 62250, Mex.

SOURCE: Journal of Biological Chemistry (2001), 276(31), 28906-28912
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In susceptible lepidopteran insects, aminopeptidase N and cadherin-like proteins are the putative receptors for Bacillus thuringiensis (Bt) toxins. Using phage display, we identified a key epitope that is involved in toxin-receptor interaction. Three different scFv mols. that bind Cry1Ab toxin were obtained, and these scFv proteins have different amino acid sequences in the complementary determinant region 3 (CDR3). Binding anal. of these scFv mols. to different members of the Cry1A toxin family and to Escherichia coli clones expressing different Cry1A toxin domains showed that the three selected scFv mols. recognized only domain II. Heterologous binding competition of Cry1Ab toxin to midgut membrane vesicles from susceptible Manduca sexta larvae using the selected scFv mols. showed that scFv73 competed with Cry1Ab binding to the receptor. The calcd. binding affinities (Kd) of scFv73 to Cry1Aa, Cry1Ab, and Cry1Ac toxins are in the range of 20-51 nM. Sequence anal. showed this scFv73 mol. has a CDR3 significantly homologous to a region present in the cadherin-like protein from M. sexta (Bt-R1), Bombyx mori (Bt-R175), and Lymantria dispar. We demonstrated that peptides of 8 amino acids corresponding to the CDR3 from scFv73 or to the corresponding regions of Bt-R1 or Bt-R175 are also able to compete with

the binding of Cry1Ab and Cry1Aa toxins to the Bt-R1 or Bt-R175 receptors. Finally, we showed that synthetic peptides homologous to Bt-R1 and scFv73 CDR3 and the scFv73 antibody decreased the in vivo toxicity of Cry1Ab to M. sexta larvae. These results show that we have identified the amino acid region of Bt-R1 and Bt-R175 involved in Cry1A toxin interaction.
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 2001:242661 CAPLUS
DOCUMENT NUMBER: 135:120855
TITLE: An improved procedure for the generation of recombinant single-chain Fv antibody fragments reacting with human CD13 on intact cells
AUTHOR(S): Peipp, M.; Simon, N.; Loichinger, A.; Baum, W.; Mahr, K.; Zunino, S. J.; Fey, G. H.
CORPORATE SOURCE: Chair of Genetics, University of Erlangen-Nurnberg, Erlangen, D 91058, Germany
SOURCE: Journal of Immunological Methods (2001), 251(1-2), 161-176
CODEN: JIMMBG; ISSN: 0022-1759
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A procedure was developed to generate recombinant single chain Fv (scFv) antibody fragments reacting with the extracellular domain of human cell surface antigen CD13 (hCD13; aminopeptidase N) on intact cells. Membrane fractions prepd. from a stably transfected hCD13-pos. murine NIH/3T3 cell line were used to immunize BALB/c mice, with the intention that hCD13 would be the major immunogenic mol. recognized by the immune system. Spleen RNA from the immunized mice served to generate a combinatorial scFv phage display library. The library was adsorbed against non-transfected NIH/3T3 or Sf21 insect cells to eliminate non-relevant binders. The supernatant was then used for panning with either hCD13-transfected Sf21 insect cells or a hCD13-expressing human leukemia-derived cell line. Therefore, the key concepts of the procedure were the presentation of hCD13 as the sole human antigen on murine NIH/3T3 cells and a screening strategy where hCD13 was the major common antigen of the material used for immunization and panning. Two different hCD13-reactive phages were isolated and the sol. scFvs were expressed in E. coli and purified. The two scFvs, anti-hCD13-1 and anti-hCD13-3, differed at four amino acid positions in their VH regions and both had high affinities for hCD13 as detd. by surface plasmon resonance (KD=7 and 33.times.10-10 M, resp.). Both efficiently recognized hCD13 on intact cells. Therefore, the procedure allowed the prodn. of

high affinity scFvs reacting with a desired antigen in its native conformation without requiring extensive purifn. of the antigen and should be useful for the prepn. of scFvs against other conformation-sensitive cell-surface antigens.
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 5
ACCESSION NUMBER: 2000:125579 CAPLUS
DOCUMENT NUMBER: 132:273986
TITLE: Aminopeptidase N is a receptor for tumor-homing peptides and a target for inhibiting angiogenesis
AUTHOR(S): Pasqualini, Renata; Koivunen, Erkki; Kain, Renate; Lahdenranta, Johanna; Sakamoto, Michiie; Stryhn, Anette; Ashmun, Richard A.; Shapiro, Linda H.; Arap, Wadih; Ruoslahti, Erkki
CORPORATE SOURCE: The Burnham Institute, La Jolla, CA, 92037, USA
SOURCE: Cancer Research (2000), 60(3), 722-727
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: AACR Subscription Office
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Phage that display a surface peptide with the NGR sequence motif home selectively to tumor vasculature in vivo. A drug coupled to an NGR peptide has more potent antitumor effects than the free drug. The authors show here that the receptor for the NGR peptides in tumor vasculature is aminopeptidase N (APN; also called CD13). NGR phage specifically bound to immunocaptured APN and to cells engineered to express APN on their surface. Antibodies against APN inhibited in vivo tumor homing by the NGR phage. Immunohistochem. staining showed that APN expression is up-regulated in endothelial cells within mouse and human tumors. In another tissue that undergoes angiogenesis, corpus luteum, blood vessels also expressed APN, but APN was not detected in blood vessels of various other normal tissues stained under the same conditions. APN antagonists specifically inhibited angiogenesis in chorioallantoic membranes and in the retina and suppressed tumor growth. Thus, APN is involved in angiogenesis and can serve as a target for delivering drugs into tumors and for inhibiting angiogenesis.
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 15 OF 17 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on

STN
ACCESSION NUMBER: 2001:46953 BIOSIS
DOCUMENT NUMBER: PREV200100046953
TITLE: Aminopeptidase A-binding peptides regulate endothelial cell function and inhibit angiogenesis.
AUTHOR(S): Marchio, S. [Reprint author]; Trepel, M.; Giordano, R.; Valdembri, D. [Reprint author]; Nanus, D.; Pasqualini, R.; Bussolino, F. [Reprint author]
CORPORATE SOURCE: Institute for Cancer Research and Treatment, University of Torino, Torino, Italy
SOURCE: Tumori, (July-August, 2000) Vol. 86, No. 4 Suppl. 1, pp. 13. print.
Meeting Info.: XV Congress of the Italian Cancer Society. Turin, Italy. October 05-07, 2000. Italian Cancer Society.
CODEN: TUMOAB. ISSN: 0300-8916.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 17 Jan 2001
Last Updated on STN: 15 Feb 2002

L5 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:194336 CAPLUS
DOCUMENT NUMBER: 130:232477
TITLE: Methods using NGR receptor binding for identifying molecules that home to angiogenic vasculature in tumors
INVENTOR(S): Ruoslahti, Erkki; Pasqualini, Renata
PATENT ASSIGNEE(S): The Burnham Institute, USA
SOURCE: PCT Int. Appl., 180 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9913329	A1	19990318	WO 1998-US18895	19980908
W: AU, CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6576239	B1	20030610	US 1997-926914	19970910
US 6180084	B1	20010130	US 1998-139802	19980825
AU 9894773	A	19990329	AU 1998-94773	19980908
EP 1015884	A1	20000705	EP 1998-948140	19980908

R: CH, DE, FR, GB, IT, LI

JP 2001516055	T	20010925	JP 2000-511062	19980908
US 6491894	B1	20021210	US 2000-659786	20000911
US 2003113320	A1	20030619	US 2002-264374	20021003
US 2004096441	A9	20040520		
US 2003152578	A1	20030814	US 2003-375992	20030227
US 2004131623	A9	20040708		

PRIORITY APPLN. INFO.: US 1997-926914 A 19970910
US 1998-139802 A 19980825
US 1996-60947P P 19960910
US 1996-710067 A 19960910
WO 1998-US18895 W 19980908
US 2000-659786 A3 20000911

AB A method is disclosed for identifying a tumor homing mol. that homes to angiogenic vasculature by contacting a substantially purified NGR receptor with one or more mols. and detg. specific binding of a mol. to the NGR receptor, where the presence of specific binding identifies the mol. as a tumor homing mol. that homes to angiogenic vasculature. The invention also provides a method of directing a moiety to angiogenic vasculature in a subject by administering to the subject a conjugate including a moiety linked to a tumor homing mol. that exhibits specific binding to an NGR receptor, whereby the moiety is directed to angiogenic vasculature. In addn., the invention provides a method of imaging the angiogenic vasculature of a tumor in a subject by administering to the subject a conjugate having a detectable moiety linked to a tumor homing mol. that exhibits specific binding to an NGR receptor and detecting the conjugate.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 17 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 6
ACCESSION NUMBER: 1993:533841 CAPLUS
DOCUMENT NUMBER: 119:133841
TITLE: Membrane topologies of the TolQ and TolR proteins of Escherichia coli: inactivation of TolQ by a missense mutation in the proposed first transmembrane segment
AUTHOR(S): Kampfenkel, Karlheinz; Braun, Volkmar
CORPORATE SOURCE: Univ. Tuebingen, Tuebingen, D-7400, Germany
SOURCE: Journal of Bacteriology (1993), 175(14), 4485-91
CODEN: JOBAAY; ISSN: 0021-9193
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The TolQ and TolR proteins of E. coli are required for the uptake of group A colicins and for infection by filamentous phages. Their topol. in the cytoplasmic membrane was detd. by cleavage with aminopeptidase K, proteinase K, and trypsin in spheroplasts and

cell lysates. From the results obtained, it is proposed that the N terminus of TolQ is located in the periplasm and that it contains three transmembrane segments (residues 9 to 36, 127 to 159, and 162 to 191), a small periplasmic loop, and two large portions in the cytoplasm. The N terminus of TolR is located in the cytoplasm and is followed by a transmembrane segment (residues 21 to 40), and the remainder of the protein is located in the periplasm. A tolQ mutant, which rendered cells resistant to group A colicins and sensitive to cholate, had alanine 13 replaced by glycine and was lacking serine 14 in the first transmembrane segment. The membrane topologies of TolQ and TolR are similar to those proposed for ExbB and ExbD, resp., which is consistent with the partial functional substitution between ExbB and TolQ and between ExbD and TolR. The amino acid sequences of these proteins display the highest homol. in the transmembrane segments, which indicates that the membrane-spanning regions play an important role in the activities of the proteins.

=> FIL STNGUIDE
COST IN U.S. DOLLARS SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST 66.64 66.85

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL
ENTRY SESSION
CA SUBSCRIBER PRICE -11.70 -11.70

FILE 'STNGUIDE' ENTERED AT 06:53:05 ON 06 SEP 2007
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COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Aug 31, 2007 (20070831/UP).

=> file caplus
COST IN U.S. DOLLARS SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST 0.78 67.63

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL
ENTRY SESSION
CA SUBSCRIBER PRICE 0.00 -11.70

FILE 'CAPLUS' ENTERED AT 07:00:46 ON 06 SEP 2007

FILE COVERS 1907 - 6 Sep 2007 VOL 147 ISS 11
FILE LAST UPDATED: 5 Sep 2007 (20070905/ED)

=> D history

(FILE 'HOME' ENTERED AT 06:43:38 ON 06 SEP 2007)

FILE 'CAPLUS, BIOSIS' ENTERED AT 06:43:55 ON 06 SEP 2007
L1 11223 PHAGE (L) DISPLAY
L2 0 AMINOPEPTIDAE (W) A
L3 27126 AMINOPEPTIDASE
L4 23 L1 AND L3
L5 17 DUPLICATE REMOVE L4 CAPLUS (6 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 06:53:05 ON 06 SEP 2007

FILE 'CAPLUS' ENTERED AT 07:00:46 ON 06 SEP 2007

=> peptide (w) inhibitor
377122 PEPTIDE
276344 PEPTIDES
483086 PEPTIDE
(PEPTIDE OR PEPTIDES)
549956 INHIBITOR
553709 INHIBITORS
863748 INHIBITOR

(INHIBITOR OR INHIBITORS)
L6 2696 PEPTIDE (W) INHIBITOR

=> L3 and L6
L7 40 L3 AND L6

=> "aminopeptidase A"
15214 "AMINOPEPTIDASE"
2634 "AMINOPEPTIDASES"
15685 "AMINOPEPTIDASE"
("AMINOPEPTIDASE" OR "AMINOPEPTIDASES")
21267875 "A"
L8 615 "AMINOPEPTIDASE A"
("AMINOPEPTIDASE"(W)"A")

=> L6 and L8
L9 2 L6 AND L8

=> D L9 IBIB ABS 1-2

L9 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:187472 CAPLUS
DOCUMENT NUMBER: 140:233520
TITLE: Aminopeptidase A is a functional target in angiogenic blood vessels
AUTHOR(S): Marchio, Serena; Lahdenranta, Johanna; Schlingemann, Reinier O.; Valdembri, Donatella; Wesseling, Pieter; Arap, Marco A.; Hajitou, Amin; Ozawa, Michael G.; Trepel, Martin; Giordano, Ricardo J.; Nanus, David M.; Dijkman, Henri B. P. M.; Oosterwijk, Egbert; Sidman, Richard L.; Cooper, Max D.; Bussolino, Federico; Pasqualini, Renata; Arap, Wadih
CORPORATE SOURCE: The University of Texas M.D. Anderson Cancer Center, Houston, TX, 77030, USA
SOURCE: Cancer Cell (2004), 5(2), 151-162
CODEN: CCAECI; ISSN: 1535-6108
PUBLISHER: Cell Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We show that a membrane-assocd. protease, aminopeptidase A (APA), is upregulated and enzymically active in blood vessels of human tumors. To gain mechanistic insight, we evaluated angiogenesis in APA null mice. We found that, although these mice develop normally, they fail to mount the expected angiogenic response to hypoxia or growth factors. We then isolated peptide inhibitors of APA from a peptide library and show that they specifically bind to and inhibit

APA, suppress migration and proliferation of endothelial cells, inhibit angiogenesis, and home to tumor blood vessels. Finally, we successfully treated tumor-bearing mice with APA binding peptides or anti-APA blocking monoclonal antibodies. These data show that APA is a regulator of blood vessel formation, and can serve as a functional vascular target.
REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1991:1192 CAPLUS
DOCUMENT NUMBER: 114:1192
TITLE: Effects of low molecular weight peptides and divalent cations on degradation and binding of angiotensin II
AUTHOR(S): Nomura, S.; Mizutani, Shigehiko; Kurauchi, O.; Kasugai, M.; Narita, O.; Tomoda, Y.
CORPORATE SOURCE: Sch. Med., Nagoya Univ., Nagoya, 466, Japan
SOURCE: Hormone and Metabolic Research (1990), 22(8), 444-8
CODEN: HMMRA2; ISSN: 0018-5043
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To det. the roles of aminopeptidase A and M on the metab. and receptor binding of angiotensin II (A-II), the effects of peptide inhibitors (bestatin and amastatin) and divalent cations (Ca2+ and Co2+) were tested on the velocity of Asp1 liberation from angiotensin II (A-II) by human placental membrane fractions at 22.degree. and 4.degree.. The binding of 125I-labeled A-II (125IA-II) to human placental membranes as thse temps. was also tested. Asp1 liberation was measured by HPLC. As expected, the degrdn. and binding of A-II were temp. sensitive, with both being less at 4.degree. than at 22.degree.. Amastatin (10-4M) and bestatin 10-6M) decreased the velocity of Asp1 liberation from A-II to about 45%, whereas amastatin (10-4M) and bestatin (10-4M) increased 125I A-II binding to 125 and 130%, resp. Ca2+ (10 mM) and Co2+ (10 mM) activated the velocity of Asp1 liberation from A-II to 140 and 120%, resp. at 22.degree.. Ca2+ (10-1M) and Co2+ (10 mM) also enhanced 125I A-II binding .apprx.130%. Aminopeptidase A and M may thus regulate the levels of A-II and, therefore, may play an important role in the binding of A-II to human placental membrane fractions.

=> receptor and L8
715204 RECEPTOR
657098 RECEPTORS
852632 RECEPTOR
(RECEPTOR OR RECEPTORS)

L10 83 RECEPTOR AND L8

=> binding (w) ligand
994145 BINDING
2160 BINDINGS
994763 BINDING
(BINDING OR BINDINGS)
327755 LIGAND
222996 LIGANDS
445946 LIGAND
(LIGAND OR LIGANDS)
L11 2725 BINDING (W) LIGAND

=> L11 and L8
L12 0 L11 AND L8

=> L11 and L6
L13 5 L11 AND L6

=> ligand and l8
327755 LIGAND
222996 LIGANDS
445946 LIGAND
(LIGAND OR LIGANDS)
L14 16 LIGAND AND L8

=> D L13 IBIB ABS 1-5

L13 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:530199 CAPLUS
TITLE: Combinatorial computational ligand design.
AUTHOR(S): Joseph-McCarthy, Diane; Hogle, James M.; Karplus, Martin
CORPORATE SOURCE: Department Biological Chemistry & Molecular Pharmacology, Harvard Medical School, Boston, MA, 02115, USA
SOURCE: Book of Abstracts, 216th ACS National Meeting, Boston, August 23-27 (1998), COMP-033. American Chemical Society: Washington, D. C.
CODEN: 66KYA2
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB A combinatorial computational approach to ligand design for large biol. systems is presented. Binding sites in the target structure are first detd. with the multiple copy simultaneous search (MCSS) method for a set of functional groups. Various strategies for connecting functional group

min. to construct possible ligands or combinatorial libraries of ligands are used. The approach is applied to the design of structure-based capsid-binding ligands for poliovirus and rhinovirus, D-peptide inhibitors of Hepatitis Delta Antigen, and to a ligand library for class II MHC mols. For poliovirus, one strategy, which introduces linker carbon atoms between selected min., has been used in the synthesis of small combinatorial libraries of ligands. Another strategy involves attaching different functional groups to mol. skeletons with the HOOK program, where the database of skeletons is selected to facilitate synthesis of the candidate ligands. The energetics of ligand and candidate ligand-receptor interactions are examd. to improve our understanding of the results.

L13 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:341592 CAPLUS
DOCUMENT NUMBER: 129:49637
TITLE: Malarial binding site on Duffy blood group protein
INVENTOR(S): Pogo, Oscar A.; Chaudhuri, Asok
PATENT ASSIGNEE(S): New York Blood Center, Inc., USA
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9821235	A1	19980522	WO 1997-US21063	19971114
W: AU, CA, CN, IL, JP, KR				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5911991	A	19990615	US 1996-749526	19961115
CA 2308833	A1	19980522	CA 1997-2308833	19971114
AU 9852622	A	19980603	AU 1998-52622	19971114

PRIORITY APPLN. INFO.: US 1996-749526 A 19961115
US 1993-140797 A2 19931021
WO 1997-US21063 W 19971114

AB A compn. and method for inhibiting binding of malarial Duffy-binding ligand to Duffy blood group antigens on mammalian erythrocytes is disclosed. The compn. includes a Duffy-related peptide which interferes with binding between Duffy antigen expressed on erythrocyte cell surfaces and the Duffy-binding ligands of merozoites. Particularly preferred peptides are the peptides having the sequences AELSPSTENSSQLDFEDVWNSSYGVNDSFPDGDYD (SEQ ID NO:1) or

AELSPSTQNSSQLNSDLWNFSYDGNDSFPDVDYD (SEQ ID NO:4), as well as peptides
which comprise either of those sequences in their primary structure, or other peptides having equiv. function. A method is disclosed which comprises administering a Duffy-based peptide which interferes with malarial binding to Duffy antigen in an amt. sufficient to inhibit binding of merozoites to erythrocytes.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:639671 CAPLUS
DOCUMENT NUMBER: 125:295928
TITLE: Synthesis and in vitro examination of type-IV collagenase
AUTHOR(S): Suli-Vargha, H.; Liko, Zs.; Botyanszki, J.
CORPORATE SOURCE: Research Group Peptide Chemistry, Hungarian Academy Sciences, Budapest, H-1518, Hung.
SOURCE: Peptides 1994, Proceedings of the European Peptide Symposium, 23rd, Braga, Port., Sept. 4-10, 1994 (1995) , Meeting Date 1994, 877-878. Editor(s): Maia, Hernani L. S. ESCOM: Leiden, Neth.
CODEN: 63MBAO
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Type IV collagenases (gelatinases) are matrix metalloproteinases. Compds. with zinc-binding ligands attached to peptide sequences recognized by this enzyme were synthesized and tested for inhibitory activity. The zinc-binding ligands used here were bis(imidazol-2-yl)methylamine (BIMA) and 3-[bis(imidazol-2-yl)]propionic acid (BIP). These ligands were coupled to cleavage products (and their analogs) of the sequence Pro-Leu-Gly-Ile-Ala-Gly. The synthesized inhibitors as well as the ligands BIP and BIM, [bis(imidazol-2-yl)methane] were tested for inhibitory activity towards a 72-kDa gelatinase. BIM was used as the control instead of BIMA because the free amino group of BIMA would have disturbed the kinetic measurements. BIP and BIM, in millimolar concns., caused a 50% inhibition in gelatinase activity; however, unexpectedly, the peptide inhibitors did not show a significant further decrease in IC50 values beyond these control values.

L13 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:380112 CAPLUS
DOCUMENT NUMBER: 122:161381
TITLE: Preparation of peptide inhibitors

of selectin binding.
INVENTOR(S): Heavner, George A.; Kruszynski, Marian
PATENT ASSIGNEE(S): Centocor, Inc., USA
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9414836	A1	19940707	WO 1993-US12110	19931213
W: CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5710123	A	19980120	US 1995-454207	19950609

PRIORITY APPLN. INFO.: US 1992-997771 A 19921218
WO 1993-US12110 W 19931213
OTHER SOURCE(S): MARPAT 122:161381
AB R1X1A1B1C1D1E1F1G1H1H1J1X2R2, R1X1-cyclo-(A2B1C1D1E1F1G1H1I2)-J1X2R2 (X1 =
N-terminal sequence of 0-10 amino acids; R1 = H, alkyl, aryl, CHO, alkanoyl, aroyl, alkoxycarbonyl, aryloxycarbonyl; X2 = C-terminal sequence of 0-10 amino acids; R2 = OH, OR3, NR5R6; R3 = alkyl, aryl; R5, R6 = H, alkyl, aryl, cycloalkyl; A1 = null, D- or L-Cys; A2 = D- or L-Cys; B1 = D- or L-His, -Ser, -Leu, -Phe, -Asn, -Pro, -Glu; C1 = D- or L-Lys, -His, -Arg, -Ser; D1 = D- or L-Lys, -Leu, -Ala, -Phe, -His, -Arg, -Ser; E1 = D- or L-Lys, -Phe, -Gln, -Arg; F1 = D- or L-His, -Leu, -Ala, -Ile, -Thr, -Arg; G1 = D- or L-Ala, -Phe, -His, -Gln; H1 = D- or L-Leu, -Phe, -Ile, -Pro, -Ala; I1 = D- or L-Cys, -Phe, -Ile, -His, -Leu, -Val, -Thr, -Ser; I2 = D- or L-Cys; J1 = D- or L-Tyr, -Phe, -Ile, -Val), were prepd. The peptides have as their core region portions of the 109-118 amino acid sequence of P-selectin, E-selectin or L-selectin. Diagnostic and therapeutic methods are given utilizing the peptides and pharmaceutical compns. thereof. Thus, Cys-Leu-Lys-Lys-Lys-His-Ala-Leu-Cys-Tyr-NH2 was prepd. using BOC-protected amino acids on methylbenzhydrylamine resin. Title compds. inhibited binding of human neutrophils to P-selectin with IC50 = 0.003-1.013 mM.

L13 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:558203 CAPLUS
DOCUMENT NUMBER: 121:158203
TITLE: Preparation of peptide inhibitors of selectin binding
INVENTOR(S): Heavner, George A.; Epps, Leon; Kruszynski, Marian
PATENT ASSIGNEE(S): Centocor, Inc., USA

SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9324526	A1	19931209	WO 1993-US3970	19930428
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 656904	A1	19950614	EP 1993-910856	19930428
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 07507302	T	19950810	JP 1993-500534	19930428
US 5602230	A	19970211	US 1995-438475	19950510

PRIORITY APPLN. INFO.: US 1992-889650 A 19920528
WO 1993-US3970 W 19930428
OTHER SOURCE(S): MARPAT 121:158203

AB R1-W-A-B-C-D-X-R2, R1-Y-E-F-G-H-Z-R2 (W, Y = N-terminal amino acid linear sequence of 0-10 amino acids; R1 is attached to the terminal .alpha.-amino group of W, Y, or the terminal .alpha.-amino group of A or E if W or Y is null; X, Z = C-terminal amino acid linear sequence of 0-10 amino acids, R2 is attached to the carboxy carbon of X or Z or the carboxy carbon of D or H if X or Z is null; A = D- or L-Tyr, D- or L-Phe, D- or L-Lys, D- or L-Glu, D- or L-Arg, D- or L-Cys, D- or L-4-aminophenylalanyl, D- or L-naphthylalanyl, D- or L-pyridylalanyl, D- or L-tetrahydroisoquinolinecarboxylate, etc.; B = D- or L-Thr, D- or L-Lys, D- or L-Glu, D- or L-Cys, Gly; C = D- or L-Asp, D- or L-His, D- or L-Glu, D- or L-Asp, D- or L-Gln, D- or L-Ala, D- or L-Phe, D- or L-Lys, Gly; D = D- or L-Val, D- or L-Ile, D- or L-Ala, D- or L-Val, Gly, D- or L-Glu, D- or L-Asp, D- or L-Asn, D- or L-Gln, D- or L-Thr, etc.; E, F, G = D- or L-Leu, D- or L-Ile, D- or L-Ala, D- or L-Val, D- or L-Glu, D- or L-Asp, D- or L-Asn, D- or L-Gln, D- or L-Thr, etc.; H = D- or L-Gln, D- or L-Glu, D- or L-Asp; R1 = H, alkyl, aryl, formyl, alkanoyl, aroyl, alkoxycarbonyl, aroyloxycarbonyl; R2 = OH, OR3, amino; R3 = alkyl, aryl; with provisos), were prepd. as selectin binding inhibitors (no data). Title compds. are claimed as inhibitors of P-, E-, and L-selectin for use in treating inflammation, coagulation, ischemia, reperfusion, sepsis, adult respiratory distress syndrome, tumor metastasis, rheumatoid arthritis, and atherosclerosis, and for detecting defective selectin-binding ligands.

=> D L14 IBIB ABS 1-16

L14 ANSWER 1 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:464251 CAPLUS
DOCUMENT NUMBER: 146:440176
TITLE: Prognosis of cancer progression in patients
INVENTOR(S): Galon, Jerome; Pages, Franck; Fridman, Wolf-Herman
PATENT ASSIGNEE(S): Institut National de la Sante et de la Recherche Medicale (INSERM), Fr.
SOURCE: PCT Int. Appl., 205pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007045996	A1	20070426	WO 2006-IB3168	20060928
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 1777523	A1	20070425	EP 2005-292200	20051019
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				

PRIORITY APPLN. INFO.: EP 2005-292200 A 20051019
US 2006-764356P P 20060202

AB The authors disclose the prognostic outcome for patients wherein the assessment is based on the quantification of one or several biol. markers that are indicative of the presence of, or alternatively the level of, the adaptive immune response in the patient. In one example, the expression of lymphocyte markers by T-cells infiltrating colon cancer biopsies was assocd. with increased survival.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:1137919 CAPLUS
DOCUMENT NUMBER: 143:400347
TITLE: Roles of brain angiotensins II and III in thirst and sodium appetite
AUTHOR(S): Wilson, Wendy L.; Roques, Bernard P.; Llorens-Cortes, Catherine; Speth, Robert C.; Harding, Joseph W.; Wright, John W.
CORPORATE SOURCE: Department of Psychology, Washington State University, Pullman, WA, 99164-4820, USA
SOURCE: Brain Research (2005), 1060(1-2), 108-117
CODEN: BRREAP; ISSN: 0006-8993
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The current study examd. the effects of intracerebroventricular (icv) infused aminopeptidase-resistant analogs of angiotensin II (AngII) and angiotensin III (AngIII) on thirst and sodium appetite. The analogs, [D-Asp1,D-Arg2]AngII and [D-Arg1]AngIII, were further protected from degrdn. by pretreatment with the aminopeptidase A inhibitor, EC 33, or the aminopeptidase N inhibitor, PC 18. Prior to icv infusions, rats were sodium depleted with furosemide, followed by the angiotensin-converting enzyme inhibitor captopril, to block endogenous angiotensin formation. Both angiotensin analogs, at either of the two doses, were capable of eliciting fluid intakes of water and 0.3 M NaCl. Water and saline intakes were increased to a similar extent by 125 and 1250 pmol of [D-Asp1,D-Arg2]AngII. [D-Arg1]AngIII produced a dose-dependent increase in water intake, whereas saline intake was equivalently increased by the 125 and 1250 pmol infusions. Pretreatment with EC 33 or PC 18 decreased water and saline intakes in response to [D-Asp1,D-Arg2]AngII, while pretreatment with PC 18 altered the time course of the [D-Arg1]AngIII-induced water and saline intakes. The ability of both inhibitors to decrease, but not completely block, AngII analog-induced intakes, coupled with the altered time course of the responses induced by the AngIII analog in the presence of PC 18, supports the hypothesis that both AngII and AngIII are active ligands in brain angiotensin-mediated thirst and sodium appetite. However, these results do not resolve the primary question of whether conversion of AngII to AngIII is a prerequisite to dipsogenic and salt appetite responses in the brain.
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:294954 CAPLUS
DOCUMENT NUMBER: 140:418229

TITLE: Sexual dimorphism of rat liver gene expression: regulatory role of growth hormone revealed by deoxyribonucleic acid microarray analysis

AUTHOR(S): Ahluwalia, Amrita; Clodfelter, Karl H.; Waxman, David J.

CORPORATE SOURCE: Division of Cell and Molecular Biology, Department of Biology, Boston University, Boston, MA, 02215, USA

SOURCE: Molecular Endocrinology (2004), 18(3), 747-760
CODEN: MOENEN; ISSN: 0888-8809

PUBLISHER: Endocrine Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB GH has diverse physiol. actions and regulates the tissue-specific expression of numerous genes involved in growth, metab., and differentiation. Several of the effects of GH on somatic growth and gene expression are sex dependent and are regulated by pituitary GH secretory patterns, which are sexually differentiated. The resultant sex differences in plasma GH profiles are particularly striking in rodents and are the major determinant of sex differences in pubertal body growth rates and the expression in liver of several cytochrome P 450 (CYP) enzymes that metabolize steroids, drugs, and environmental chems. of importance to endocrinol., pharmacol., and toxicol. DNA microarray anal. was used to identify rat liver-expressed genes that show sexual dimorphism, and to ascertain the role of GH as a regulator of their sexually dimorphic expression. Adult male and female rats were untreated or were treated with GH by 7-d continuous infusion using an Alzet osmotic minipump. Poly(A) RNA was purified from individual livers and Cy3- and Cy5-labeled cDNA probes co-hybridized to Pan Rat Liver and 5K Rat Oligonucleotide microarrays representing 5889 unique rat genes. Anal. of differential gene expression profiles identified 37 liver-expressed, female-predominant genes; of these, 27 (73%) were induced by continuous GH treatment of male rats. Moreover, only three of 30 genes up-regulated in male rat liver by continuous GH treatment did not display female-dominant expression. Further anal. revealed that 44 of 49 male-predominant genes (90%) were down-regulated in the livers of continuous GH-treated male rats compared with untreated male rats, whereas only five of 49 genes that were down-regulated in male rats by continuous GH treatment were not male dominant in their expression. Real-time PCR anal. applied to a sampling of 10 of the sexually dimorphic genes identified in the microarray anal. verified their sex- and GH-dependent patterns of regulation. Taken together, these studies establish that GH-regulated gene expression is the major mechanistic determinant of sexually dimorphic gene expression in the rat liver model.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:892932 CAPLUS
DOCUMENT NUMBER: 139:374995
TITLE: Vascular targeting of cytokine-tumor targeting moiety immunoconjugates enhances chemotherapy drug penetration into tumors without increased toxicity and is used in cancer diagnosis and treatment
INVENTOR(S): Corti, Angelo; Curnis, Flavio
PATENT ASSIGNEE(S): Molmed S.p.A., Italy
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003093478	A1	20031113	WO 2003-IB2187	20030430
WO 2003093478	A9	20041209		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2462879	A1	20031113	CA 2003-2462879	20030430
AU 2003228057	A1	20031117	AU 2003-228057	20030430
EP 1499730	A1	20050126	EP 2003-725526	20030430
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005526117	T	20050902	JP 2004-501614	20030430
CN 1665933	A	20050907	CN 2003-815079	20030430
US 2005033026	A1	20050210	US 2004-492117	20040917
IN 2004CN02464	A	20070302	IN 2004-CN2464	20041029
NO 2004005237	A	20050128	NO 2004-5237	20041129

PRIORITY APPLN. INFO.: GB 2002-9896 A 20020430
WO 2003-IB2187 W 20030430

AB This invention relates to vascular targeting of cytokine-tumor targeting moiety immunoconjugates for enhanced chemotherapy drug penetration into tumors without increased toxicity and is used in cancer diagnosis and

treatment. A fusion protein linking a cytokine fragment and a tumor targeting moiety (ex. tumor necrosis factor) is developed and administered to mice bearing tumors. The fusion protein, targeted to the tumor, influences the tumor blood barrier such that subsequent administration of chemotherapeutic drug (ex. cisplatin) has enhanced penetration of the tumor. Efficacy studies in tumor-bearing mice show a complex drug response curve, with highest efficacy using either very low doses or very high doses of fusion protein. Very low doses appear to be preferential as they do not activate a neg. feedback mechanism to block further drug uptake and show no significant toxicity. Neg. feedback is believed to be due to sol. receptor shedding in tumor blood vessels. This fusion protein used in conjunction with chemotherapeutic agents is designed for the purpose of enhanced cancer diagnosis and therapy in humans.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:892647 CAPLUS
DOCUMENT NUMBER: 139:380023
TITLE: Fusion proteins contg. cytokines and tumor targeting moieties and uses thereof in diagnosis and antitumor therapy
INVENTOR(S): Corti, Angelo; Curnis, Flavio
PATENT ASSIGNEE(S): Molmed S.p.A., Italy
SOURCE: PCT Int. Appl., 104 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003092737	A1	20031113	WO 2003-IB2515	20030430
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2484425	A1	20031113	CA 2003-2484425	20030430

AU 2003236969 A1 20031117 AU 2003-236969 20030430
EP 1499362 A1 20050126 EP 2003-735883 20030430
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
JP 2005525115 T 20050825 JP 2004-500920 20030430
CN 1665543 A 20050907 CN 2003-815203 20030430
US 2005074426 A1 20050407 US 2004-492144 20040809
IN 2004CN02465 A 20070803 IN 2004-CN2465 20041029
NO 2004005236 A 20050131 NO 2004-5236 20041129
PRIORITY APPLN. INFO.: GB 2002-9893 A 20020430
WO 2003-IB2515 W 20030430

AB The disclosed invention relates to a conjugate which is a mol. comprising at least one tumor targeting moiety (TTM)/polypeptide linked to at least one cytokine formed via genetic fusion or chem. coupling. In the preferred embodiment a conjugate is provided between tumor necrosis factor .alpha. and TNF.beta. and an NGR-contg. or an RGD-contg. peptide sequence (TTM) in which the conjugate is in the form of a fusion protein. The present invention encompasses targeting TTM to tumor cells directly or to its vasculature. In a preferred embodiment the TTM is a ligand for .alpha.v.beta.3 or .alpha.v.beta.5 integrin. The examples disclose the prepn. of murine recombinant TNF and RGD-TNF, in vitro cytotoxic activity of TNF and RGD-TNF, and the antitumor activity and toxicity of RGD-TNF compared to TNF using the RMA T lymphoma and the T/SA models in C57BL6 mice.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 6 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:253505 CAPLUS
DOCUMENT NUMBER: 139:47549
TITLE: Conversion of brain angiotensin II to angiotensin III is critical for pressor response in rats
AUTHOR(S): Wright, John W.; Tamura-Myers, Elizabeth; Wilson, Wendy L.; Roques, Bernard P.; Llorens-Cortes, Catherine; Speth, Robert C.; Harding, Joseph W.
CORPORATE SOURCE: Department of Psychology, Program in Neuroscience, Washington State University, Pullman, WA, 99164-4820, USA
SOURCE: ~~American Journal of~~ Physiology (2003), 284(3, Pt. 2), R725-R733
CODEN: AJPHAP; ISSN: 0002-9513
PUBLISHER: American Physiological Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The present investigation measured the relative pressor potencies of

intracerebroventricularly infused ANG II, ANG III, and the metabolically resistant analogs D-Asp1ANG II and D-Arg1ANG III in alert freely moving rats. The stability of these analogs was further facilitated by pretreatment with the specific aminopeptidase A inhibitor EC33 or the aminopeptidase N inhibitor PC18. The results indicate that the max. elevations in mean arterial pressure (MAP) were very similar for each of these compds. across the dose range 1, 10, and 100 pmol/min during a 5-min infusion period. However, D-Asp1ANG II revealed significantly extended durations of pressor effects before return to base level MAP. Pretreatment intracerebroventricular infusion with EC33 blocked the pressor activity induced by the subsequent infusion of D-Asp1ANG II, whereas EC33 had no effect on the pressor response to subsequent infusion of D-Arg1ANG III. In contrast, pretreatment infusion with PC18 extended the duration of the D-Asp1ANG II pressor effect by about 2-3 times and the duration of D-Arg1ANG III's effect by .apprx.10-15 times. Pretreatment with the specific AT1 receptor antagonist losartan blocked the pressor responses induced by the subsequent infusion of both analogs indicating that they act via the AT1 receptor subtype. These results suggest that the brain AT1 receptor may be designed to preferentially respond to ANG III, and ANG III's importance as a centrally active ligand has been underestimated.

REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:220823 CAPLUS
DOCUMENT NUMBER: 136:261809
TITLE: Identifying T cell and antigen recognition epitopes by positional scanning synthetic combinatorial libraries and artificial neural network
INVENTOR(S): Martin, Roland; Simon, Richard; Zhao, Yingdong; Gran, Bruno; Pinilla, Clemencia
PATENT ASSIGNEE(S): United States, Department of Health and Human Services, USA
SOURCE: PCT Int. Appl., 97 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022860	A2	20020321	WO 2001-US42166	20010911
WO 2002022860	A9	20021031		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2422122	A1	20020321	CA 2001-2422122	20010911
AU 2001093281	A5	20020326	AU 2001-93281	20010911
US 2004072246	A1	20040415	US 2003-380147	20031022

PRIORITY APPLN. INFO.: US 2000-232101P P 20000912
US 2000-251216P P 20001129
WO 2001-US42166 W 20010911

AB Described is a system and method comprises positional scanning synthetic combinatorial libraries or PS-SCL, artificial neural network, cDNA microarray anal., and RT-PCR-single strand conformation polymorphism for identifying T cell and other epitopes and the like. Thus, proliferative response of T cell clones GP5F11 (specific for influenza virus hemagglutinin peptide HA308-317) and TL3A6 (specific for myeline basic protein peptide MBP89-98) to 200 mixts. of a decapeptide PS-SCL was analyzed. The proliferative response of T cell clones to PS-SCL is analyzed by quantitating TCR recognition of antigens or autoantigens by clonotypic T cell.

L14 ANSWER 8 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:185320 CAPLUS
DOCUMENT NUMBER: 136:242932
TITLE: Identification of peptide ligands for specific cell types by phage display for use in drug targeting and control of biological processes
INVENTOR(S): Arap, Wadih; Pasqualini, Renata
PATENT ASSIGNEE(S): Board of Regents, the University of Texas System, USA
SOURCE: PCT Int. Appl., 311 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002020769	A1	20020314	WO 2001-US27692	20010907
WO 2002020769	A9	20030904		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2421271 A1 20020314 CA 2001-2421271 20010907

AU 200188843 A 20020322 AU 2001-88843 20010907

EP 1322755 A1 20030702 EP 2001-968603 20010907

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

JP 2004508045 T 20040318 JP 2002-525776 20010907

CA 2458047 A1 20030320 CA 2002-2458047 20020830

WO 2003022991 A2 20030320 WO 2002-US27836 20020830

WO 2003022991 A3 20041028

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002323543 A1 20030324 AU 2002-323543 20020830

EP 1497314 A2 20050119 EP 2002-757531 20020830

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

CA 2496938 A1 20040311 CA 2002-2496938 20021030

WO 2004020999 A1 20040311 WO 2002-US34987 20021030

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002364501 A1 20040319 AU 2002-364501 20021030

EP 1546714 A1 20050629 EP 2002-799873 20021030

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

US 2004170955	A1	20040902	US 2003-363204	20031006
US 2005003466	A1	20050106	US 2004-784537	20040223
US 2006094672	A1	20060504	US 2004-489071	20041013
US 2006239968	A1	20061026	US 2006-530168	20060223

PRIORITY APPLN. INFO.: US 2000-231266P P 20000908
US 2001-765101 A 20010117
WO 2001-US27692 W 20010907
WO 2002-US27836 W 20020830
WO 2002-US34987 W 20021030

AB The present invention concerns methods and compns. for in vivo and in vitro targeting. A large no. of targeting peptides directed towards human organs, tissues or cell types are disclosed. The peptides are of use for targeted delivery of therapeutic agents, including but not limited to gene therapy vectors. A novel class of gene therapy vectors is disclosed. Certain of the disclosed peptides have therapeutic use for inhibiting angiogenesis, inhibiting tumor growth, inducing apoptosis, inhibiting pregnancy or inducing wt. loss. Methods of identifying novel targeting peptides in humans, as well as identifying endogenous receptor-ligand pairs are disclosed. Methods of identifying novel infectious agents that are causal for human disease states are also disclosed. A novel mechanism for inducing apoptosis is further disclosed.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 9 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:635393 CAPLUS
DOCUMENT NUMBER: 135:327446
TITLE: Physiological significance of conversion of angiotensin II to III by aminopeptidase A
AUTHOR(S): Wright, John W.; Harding, Joseph W.; Mizutani, Shigehiko
CORPORATE SOURCE: Department of Psychology, Washington State University, Pullman, WA, 99164-4820, USA
SOURCE: International Congress Series (2001), 1218(Cell-Surface Aminopeptidases: Basic and Clinical Aspects), 39-54
CODEN: EXMDA4; ISSN: 0531-5131
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with refs. Substantial evidence suggests the presence of precursors and enzymes necessary for the formation and degrdn. of biol.

active forms of angiotensins in brain tissues. Two specific binding sites have been identified that are activated by these angiotensin ligands. The authors present the hypothesis that angiotensin II (AngII) must be converted to Angiotensin III (AngIII) to bind at the AT1 and AT2 receptor subtypes. The AT1 site mediates the classic functions concerned with the control of blood pressure, vasopressin release, body water balance, and cyclicity of reproductive hormones and sexual behaviors. The AT2 receptor subtype appears to mediate blood flow, antiangiogenesis, antifibrosis and stimulates apoptosis. Aminopeptidase A (APA) is primarily responsible for cleavage of N-terminal glutamyl and aspartyl residues from peptide substrates, and is therefore a very important enzyme in the formation of AngIII. Interference with APA activity reduces conversion of AngII to AngIII and attenuates activation of the brain AT1 receptor subtype. Thus, APA may serve as a clin. relevant target in the control of hypertension.
REFERENCE COUNT: 141 THERE ARE 141 CITED REFERENCES AVAILABLE FOR
THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:507485 CAPLUS
DOCUMENT NUMBER: 131:307428
TITLE: Participation of angiotensin receptors in acute hypoxia in mice. I. Effects of angiotensin peptide receptor ligands saralasin and sarmesin
AUTHOR(S): Georgiev, V.; Opitz, M.
CORPORATE SOURCE: Laboratory of Experimental Psychopharmacology, Institute of Physiology, Bulgarian Academy of Sciences, Sofia, Bulg.
SOURCE: Methods and Findings in Experimental and Clinical Pharmacology (1999), 21(6), 415-419
CODEN: MFEPDX; ISSN: 0379-0355
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of angiotensin II (Ang II) and angiotensin receptor ligands sarmesin ([Sar1, Tyr(Me)4] Ang II) and saralasin ([Sar1, Ala8] Ang II) administered intracerebroventricularly (i.c.v.) on acute anoxic hypoxia were studied in mice. The interactions of these ligands and of amastatin (an aminopeptidase A inhibitor) after pretreatment with Ang II and sarmesin, resp., were also studied. Ang II decreased the latency to hypoxia-induced convulsive seizures and altered survival time (increase or decrease depending on the dose). Sarmesin and saralasin significantly increased the latency to seizures as well as survival time. Pretreatment with saralasin and

sarmesin antagonized the Ang II effect on the latency to seizures. Both drugs increased the Ang II effect on the survival time. Amastatin tended to increase the effect of sarmesin on the survival time. Taken together, the results suggest that the antihypoxic effect of sarmesin and saralasin is most likely due to an action on Ang II receptors, with the agents behaving as partial agonists.
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 11 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:395170 CAPLUS
DOCUMENT NUMBER: 131:181558
TITLE: 1-Butaneboronic acid binding to Aeromonas proteolytica aminopeptidase: A case of arrested development
AUTHOR(S): De Paola, Carin C.; Bennett, Brian; Holz, Richard C.; Ringe, Dagmar; Petsko, Gregory A.
CORPORATE SOURCE: Rosenstiel Basic Medical Sciences Research Center, Brandeis University, Waltham, MA, 02454, USA
SOURCE: Biochemistry (1999), 38(28), 9048-9053
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Hydrolases contg. 2 metal cations connected by a bridging ligand catalyze reactions important in carcinogenesis, tissue repair, post-translational modification, control and regulation of biochem. pathways, and protein degrdn. The aminopeptidase (AAP) from A. proteolytica serves as a paradigm for the study of such bridged bimetallic proteases since its 3-dimensional structure is known to very high resoln. and its catalytic reaction is amenable to spectroscopic examn. Here, the authors report the x-ray crystal structure at 1.9 .ANG. resoln. of AAP complexed with 1-butaneboronic acid (BuBA). This structure suggests that this complex represents a snapshot of the proteolytic reaction in an arrested form between the Michaelis complex and the transition state. Comparison of the structure with spectroscopic and other data allowed the authors to conclude that the apparently structurally sym. di-Zn site was actually asym. electrostatically.
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:233474 CAPLUS
DOCUMENT NUMBER: 124:311054

TITLE: Identification of glutamate residues essential for catalytic activity and zinc coordination in aminopeptidase A
AUTHOR(S): Vazeux, Gilles; Wang, Jiyang; Corvol, Pierre; Llorens-Cortes, Catherine
CORPORATE SOURCE: Coll. France, INSERM, Paris, 75005, Fr.
SOURCE: Journal of Biological Chemistry (1996), 271(15), 9069-74
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Aminopeptidase A (EC 3.4.11.7, APA) is a homodimeric membrane-bound glycoprotein that contains the consensus sequence HEXXH (385-389) found in zinc metallopeptidases such as thermolysin. The x-ray structure of the latter enzyme revealed that the two histidines of this motif are two of the three zinc-coordinating ligands and that the glutamate is a crucial amino acid involved in catalysis. Alignment of the sequence of mouse APA with those of the already characterized metallopeptidases showed the presence of several conserved amino acids such as a glutamate residue in position 408 which may constitute the putative third zinc ligand. The functional implication of this residue and the role of glutamate 386 in the HELVH (385-389) motif of APA have been investigated by replacing these residues with an aspartate (Asp-386, Asp-408) or an alanine (Ala-386, Ala-408) by site-directed mutagenesis. Expressed mutated proteins in position 386 showed no APA activity. Ala-408 was also inactive, and Asp-408 had 5% of the wild type enzyme activity and a similar Km. 65Zn incorporation measurements indicated that Ala-386 binds the zinc ion as well as the wild type enzyme, whereas the Ala-408 mutant did not. These results provide evidence that Glu-408 is the third zinc-coordinating residue of APA, confirm the presumed involvement of Glu-386 in the catalytic process of the enzyme, and identify APA as a zinc metallopeptidase functionally similar to thermolysin.

L14 ANSWER 13 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:17873 CAPLUS
DOCUMENT NUMBER: 122:49931
TITLE: Crystal structure of Aeromonas proteolytica aminopeptidase: a prototypical member of the co-catalytic zinc enzyme family
AUTHOR(S): Chevrier, Bernard; Schalk, Celine; D'Orchymont, Hugues; Rondeau, Jean Michel; Moras, Dino; Tarnus, Celine
CORPORATE SOURCE: Lab. Biol. Struct., Inst. Biol. Mol. Cell.,

Strasbourg, 67084, Fr.
SOURCE: Structure (Cambridge, MA, United States) (1994), 2(4), 283-91
CODEN: STRUE6; ISSN: 0969-2126
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Aminopeptidases specifically cleave the amino-terminal residue from polypeptide chains and are involved in the metab. of biol. active peptides. The family includes zinc-dependent enzymes possessing either one or two zinc ions per active site. Structural studies providing a detailed view of the metal environment may reveal whether the one-zinc and two-zinc enzymes constitute structurally and mechanistically distinct subclasses, and what role the metal ions play in the catalytic process. We have solved the crystal structure of the monomeric aminopeptidase from Aeromonas proteolytica at 1.8 .ANG. resoln. The protein is folded into a single .alpha./.beta. globular domain. The active site contains two zinc ions (3.5 .ANG. apart) with shared ligands and sym. coordination spheres. We have compared it with the related bovine lens leucine aminopeptidase and the cobalt-contg. Escherichia coli methionine aminopeptidase. The environment and coordination of the two zinc ions in A. proteolytica aminopeptidase strongly support the view that the two metal ions constitute a co-catalytic unit and play equiv. roles during catalysis. This conflicts with the conclusions drawn from the related bovine leucine aminopeptidase and early biochem. studies. In addn., the known specificity of the aminopeptidase for hydrophobic amino-terminal residues is reflected in the hydrophobicity of the active site cleft.

L14 ANSWER 14 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:46582 CAPLUS
DOCUMENT NUMBER: 120:46582
TITLE: Characterization of the tachykinin neurokinin-2 receptor in the human urinary bladder by means of selective receptor antagonists and peptidase inhibitors
AUTHOR(S): Giuliani, Sandro; Patacchini, Riccardo; Barbanti, Gabriele; Turini, Damiano; Rovero, Paolo; Quartara, Laura; Giachetti, Antonio; Maggi, Carlo Alberto
CORPORATE SOURCE: Pharmacol. Dep., Univ. Ferrara, Florence, Italy
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1993), 267(2), 590-5
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The tachykinin (NK2) receptor-mediating contraction of the human isolated bladder to neurokinin A (NKA) was investigated by studying the affinities of eight structurally different receptor-selective antagonists (linear

peptides, cyclic peptides and pseudopeptides, non-peptide NK2 receptor antagonists). The affinities of the antagonists were compared to those measured for the same ligands at the NK2 receptors previously characterized in the rabbit pulmonary artery and hamster trachea. In the presence of a cocktail of peptidase inhibitors (bestatin, captopril and thiorphan, 1 .mu.M each) no significant correlation was found between pA2 values measured in the human bladder vs. those measured in the other two NK2 receptor-bearing prepns. In the presence of the aminopeptidase inhibitor amastatin, however, pA2 values of the linear antagonists bearing an N-terminal Asp residue, MEN 10,207 and MEN 10,376, were significantly enhanced and these pA2 values were used for anal.; a significant correlation was found between pA2 values measured in the human urinary bladder and rabbit pulmonary artery. The pseudopeptide analog of NKA (4-10), MDL 28,564, (which also bears a N-terminal Asp residue) behaved as an agonist and its action was enhanced by amastatin. The NK2 receptor-mediating contraction of the human urinary bladder smooth muscle is similar to that previously characterized in the rabbit pulmonary artery (NK2A receptor category); in the human bladder smooth muscle an amastatin-sensitive peptidase (possibly aminopeptidase A) limits biol. activity of linear peptide derivs. of NKA bearing a N-terminal Asp residue.

L14 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1990:435346 CAPLUS
DOCUMENT NUMBER: 113:35346
TITLE: Intracerebroventricularly infused [D-Arg1]angiotensin III, is superior to [D-Asp1]angiotensin II, as a pressor agent in rats
AUTHOR(S): Wright, John W.; Roberts, Kim A.; Cook, Vickie I.; Murray, Cathy E.; Sardinia, Michael F.; Harding, Joseph W.
CORPORATE SOURCE: Dep. Psychol., Washington State Univ., Pullman, WA, 99164, USA
SOURCE: Brain Research (1990), 514(1), 5-10
CODEN: BRREAP; ISSN: 0006-8993
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Two D-amino acid substitution angiotensin analogs were compared against native angiotensin II (AII) and angiotensin III (AIII) for their resistance to brain tissue-induced degrdn. and for pressor potency when intracerebroventricularly (i.c.v.) infused in Sprague-Dawley rats. The in vitro results indicate that [D-Asp1]AII was very resistant to degrdn., AII and [D-Arg1]AIII were degraded at similar rates, whereas AIII was the most rapidly degraded. In vivo results revealed that AII, AIII and [D-Arg1]AIII produced greater pressor responses than [D-Asp1]AII. Intracerebroventricular pretreatment with the aminopeptidase

A inhibitor, amastatin, reduced the subsequent pressor response to i.c.v. infused [D-Asp1]AII presumably by inhibiting its conversion to AIII. In contrast, pretreatment with the aminopeptidase B inhibitor, bestatin, potentiated the subsequent pressor responses to i.c.v. infused [D-Arg1]AIII, presumably by inhibiting the conversion of [D-Arg1]AIII to the less active hexapeptide AII(3-8). Next, i.c.v. pretreatment with the specific angiotensin receptor antagonist, [Sar1,Thr8]AII (Sarthran) greatly diminished the subsequent pressor responses to i.c.v. infused [D-Asp1]AII and [D-Arg1]AIII, suggesting that these analogs are having their effect at the same brain angiotensin receptor site. Thus, AIII, or AIII-like ligands, may serve as the active form of brain angiotensin.

L14 ANSWER 16 OF 16 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1986:17202 CAPLUS
DOCUMENT NUMBER: 104:17202
TITLE: Characterization of some proteins in nerve tissue using group-specific sorbents
AUTHOR(S): Zhernosekov, D. D.; Berezin, V. A.; Reva, A. D.
CORPORATE SOURCE: USSR
SOURCE: Ukrainskii Biokhimicheskii Zhurnal (1978-1999) (1985), 57(6), 9-13
CODEN: UBZHD4; ISSN: 0201-8470
DOCUMENT TYPE: Journal
LANGUAGE: Russian
AB Group-specific immobilized ligands were used for characterization of physicochem. properties of isolated sol. and membrane-bound forms of brain aminopeptidases and specific glial fibrillary acid proteins. For aminopeptidases, a microscale column chromatog. with phenyl-Sepharose and Con A-Sepharose was used. It was shown that the membrane-bound aminopeptidase is a glycoprotein which is capable to hydrophobic interactions. The sol. forms of aminopeptidase did not interact with Con A or Ph residues. the presence of hydrophobic domains was also obsd. on the surface of the glial acidic proteins. The applied methods may be useful in purifn. of enzymes and other proteins.

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ENTRY SESSION

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